PREVENTION OF INSULIN-DEPENDENT DIABETES, COMPLICATIONS THEREOF, OR ALLOGRAFT REJECTION BY INHIBITION CYCLOOXYGENASE-2 ACTIVITY

ABSTRACT OF THE DISCLOSURE

Insulin-dependent diabetes mellitus (IDDM) is an autoimmune disease believed to be caused by an inflammatory process in the pancreas leading to selective destruction of the β cells. Inducible cyclooxygenase (COX-2) is expressed under inflammatory conditions and its product prostaglandin E_2 (PGE_2) is an important inflammation mediator. Administration of the selective COX-2 inhibitor such as, e.g., NS-398 prevents the onset of diabetes in mice brought on by multiple low-doses of streptozotocin (STZ). Histological observations indicated that STZ-mediated destruction of β cells was prevented by NS-398 treatment. Delayed (day 3) administration of NS-398 was also protective in this model. These results demonstrate the critical importance of COX-2 activity in autoimmune destruction of β cells, and point to the fact that COX-2 inhibition should provide a preventive therapy against IDDM or other autoimmune problems, including allograft rejection. Inhibitors of NF-κB activation may also be used to prevent IDDM and allograft rejection.